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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/555,109	12/13/2006	Jian-Yun Dong	MESC:014US/10511807	5410

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EXAMINER	
HIRIYANNA, KELAGINAMANE T	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
09/30/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

aopatent@fulbright.com

Office Action Summary	Application No.	Applicant(s)	
	10/555,109	DONG ET AL.	
	Examiner	Art Unit	
	KELAGINAMANE HIRIYANNA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on *07/02/2010* in response to office action mailed on 01/05/2010 has been acknowledged.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

Withdrawn: Claim 13 rejection under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons of record as set forth in the office action mailed on 01/05/2010 is withdrawn in view of Applicants amendments to overcome the rejection.

Withdrawn: Claims 1-19 rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record as set forth in the office action mailed on 01/05/2010 is withdrawn in view of Applicants amendments to overcome the rejection.

Withdrawn: Claims 1, 5-19 rejection under 102(b) as being anticipated by Rubinchik et al., (2001, Molecular Therapy 4:416-426; art of record) for the reasons of record as set forth in the office action mailed on 01/05/2010 is withdrawn in view of Applicants amendments to overcome the rejection and further in view of a 103 rejection below.

Withdrawn: Claims 1-19 are rejected under 35USC102(e) & 103(a) as being anticipated by or obvious over Phillips et al., (US 2004/0161847) for the reasons of record as set forth in the office action mailed on 01/05/2010 is withdrawn in view of Applicants amendments to overcome the rejection and further in view of a revised103 rejection below.

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 5-19 are rejected under 102(e) as being anticipated by Vile et al., (Patent No.: US 6867036 B1).

The above claims are drawn to an expression vector comprising a first expression cassette encoding a transcriptional activating factor under the transcriptional control of a first promoter comprising a tissue specific regulatory element and a transcriptional activator binding site that binds the encoded TAF and a second expression cassette that encodes a selected peptide under the transcriptional control of a second promoter comprising a tissue specific regulatory element and a transcriptional activator binding site that binds the TAF encoded by the first expression cassette or only a transcriptional activator binding site that binds the TAF encoded by the first expression cassette.

Viles teaches an expression vector comprising expression cassettes, the first expression cassette comprises HSF-1 (heat shock factor-1, a TAF) under the transcriptional control of tissue specific promoter with a TSRE namely Tyr-300 (an regulated human tyrosinase promoter, a tissue specific promoter which is only active melanoma cells) and said promoter has HSE as transcriptional activator binding site (heat shock element that binds HSF-1) that binds the encoded HSF-1 generating a positive feedback loops of transcription regulation (see entire article; abstract, Fig.6 and Fig.11) for the efficient expression of a therapeutic gene as well as the TAF. Viles construct thus has both the first and second coding region controlled same regulatory loop. Viles further teaches using both plasmid and viral vectors for the same.(col.6-20). Thus the claimed invention is within the scope of Vile's disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made..

Claims 1-19 are rejected under 35 USC 103 (a) as being unpatentable over Phillips et al., (US 2004/0161847; art of record) in view of Vile et al., (Patent No.: US 6867036 B1). .

The above claims are drawn to an expression vector comprising a first expression cassette encoding a transcriptional activating factor under the transcriptional control of a first promoter comprising a tissue specific regulatory element and a transcriptional activator binding site that binds the encoded TAF and a second expression cassette that encodes a selected peptide under the transcriptional control of a second promoter comprising a tissue specific regulatory element and a transcriptional activator binding site that binds the TAF encoded by the first expression cassette or only a transcriptional activator binding site that binds the TAF encoded by the first expression cassette.

Phillips teaches "vigilant vectors system" with a single or double vector comprising expression cassettes comprising coding regions that encode a transcriptional activating factors (example oxygen sensitive transactivator under a tissue specific promoter of hMLC gene (which consists of a TAF binding site) and the second cassette that comprises nucleotide sequence encoding a therapeutic gene (e.g. a cardioprotective gene) under the control of a transactivator inducible promoter that contained a TAF binding site. Phllips however, teaches a strategy placing the two cassettes one encoding the transactivator and the other encoding the therapeutic peptide on two different plasmids or viral vectors and their co-transfection to cells for amplified tissue specific expression (p.265, col.2, 2nd paragraph). However given the general knowledge in the prior art regarding gene expression construct technology at the time of invention, the two cassettes could have been expressed to achieve the same result by incorporating them in to a single vector molecule. Phillips however, does not teach expression construct where the encoded TAF

of the first cassette binds to TBS of both the first and second cassette to regulate the expression by autofeed back.

Viles teaches the advantages of a autofeed back mechanism in an expression vector comprising expression cassettes, the first expression cassette comprises HSF-1 (heat shock factor-1, a TAF) under the transcriptional control of tissue specific promoter with a TSRE namely Tyr-300 (an regulated human tyrosinase promoter, a tissue specific promoter which is only active melanoma cells) and said promoter has HSE as transcriptional activator binding site (heat shock element that binds HSF-1) that binds the encoded HSF-1 generating a positive feedback loops of transcription regulation (see entire article; abstract, Fig.6 and Fig.11) for the efficient expression of a therapeutic gene as well as the TAF. Viles construct thus has both the first and second coding region controlled same regulatory loop. Vile's further teaches using both the plasmid and viral vectors for the same.(col.6-20).

Thus it would have been obvious for one of ordinary skill in the art to incorporate a autofeed bcak loop for regulating the expression of the genes in the two plasmid or viral vigilant system of Phllips that upregulates the tissue specific expression of a therapeutic gene in to a single plasmid or viral vector comprising both the cassettes for transactivator amplification and tissue specific expression by adding theTRE to the promoter of both the TBS and therapeutic gene following the teachings of Vile. One of skill in the art would have been motivated to incorporate a autofeed back loop of the TAF to increase the efficiency of expression of a gene under a promoter. One of ordinary skill in the art would have reasonable expectation of success making using a vector system for expressing both the transactivator and therapeutic gene under the same tissue specific promoter with a TRE that binds the encoded TBS for the efficient expression of the therapeutic poly peptide because the art at the time of invention teaches that is it is routine to use a single vector constructs with dual expression cassettes for co-operative or co-ordinate expression and further art teaches how to make constructs with a auto feed back regulation loop for the expression of a gene in a target cell. Thus, the claimed invention was *prima facie* obvious.

Claims 1-19 are rejected under 35 USC 103 (a) as being unpatentable over Rubinchik et al., (2001, Molecular Therapy 4:416-426; art of record) in view of Vile et al., (Patent No.: US 6867036 B1). .

The above claims are drawn to an expression vector comprising a first expression cassette encoding a transcriptional activating factor under the transcriptional control of a first promoter comprising a tissue specific regulatory element and a transcriptional activator binding site that binds the encoded TAF and a second expression cassette that encodes a selected peptide under the transcriptional control of a second promoter comprising a tissue specific regulatory element and a transcriptional activator binding site that binds the TAF encoded by the first expression cassette or only a transcriptional activator binding site that binds the TAF encoded by the first expression cassette.

Rubinchik teaches an Adenoviral expression vector comprising two expression cassettes, the first expression cassette comprises tetracycline transactivator gene (a TAF) under the transcriptional control of ARR2PB promoter (an androgen regulated prostate tissue specific promoter) and said promoter comprises a transcriptional activator binding site and the second expression cassette comprises Tnfsf6-GFP fusion gene (encoding a tumor therapeutic polypeptide, an inducer of apoptosis) under the transcriptional control a tetracycline responsive promoter comprising teteracycline transactivator binding site.(entire article; abstract; p.418, col.2 bridging p.419-424). Rubinchik teaches replication-deficient and conditionally replication-competent Adenoviral viral vector constructs and viral particles (entire article; p.417 Fig.1). Rubinchik however, does not teach expression construct where the encoded TAF of the first cassette binds to TBS of both the first and second cassette to regulate the expression by autofeed back.

Viles teaches the advantages of a autofeed back mechanism in an expression vector comprising expression cassettes, the first expression cassette comprises HSF-1 (heat shock factor-1, a TAF) under the transcriptional control of tissue specific promoter with a TSRE namely Tyr-300 (an regulated human tyrosinase promoter, a tissue specific promoter which is only active melanoma cells) and said promoter has HSE as

transcriptional activator binding site (heat shock element that binds HSF-1) that binds the encoded HSF-1 generating a positive feedback loops of transcription regulation (see entire article; abstract, Fig.6 and Fig.11) for the efficient expression of a therapeutic gene as well as the TAF. Viles construct thus has both the first and second coding region controlled same regulatory loop. Vile's further teaches using both the plasmid and viral vectors for the same.(col.6-20).

Thus it would have been obvious for one of ordinary skill in the art to incorporate a autofeed bcak loop for regulating the expression of the genes in the construct of Rubinchik by operably including in the tissue specific promoter used for gene expression, a TBS (TRE in case of Rubinchik) that binds the encoded TAF (tetracycline transactivator(tTA) in case of Rubinchik) following the teachings of Vile. One of skill in the art would have been motivated to incorporate a autofeed back loop of the TAF to increase the efficiency of expression of a gene under a promoter. One of ordinary skill in the art would have reasonable expectation of success making using a vector system for expressing both the transactivator and therapeutic gene under the same tissue specific promoter with a TRE that binds the encoded TBS as a auto regulatory feed back for efficient expression of therapeutic poly peptide because the art at the time of invention teaches that is it is routine to use a single vector constructs with dual expression cassettes for co-operative or co-ordinate expression and further art teaches how to make constructs with a auto feed back regulation loop for the expression of a gene in a target cell. Thus, the claimed invention was *prima facie* obvious.

Conclusion:

No claim allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna Ph.D.,* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Thursday from 9 AM-7PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.,* may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

/Robert M Kelly/
Primary Examiner, Art Unit 1633